

## CLAIMS

- Sub B1
1. A method of detecting the presence of detergent- or urea-insoluble amyloid-like fibrils or protein aggregates on a filter comprising the following steps:
    - (a) contacting said filter with material suspected to comprise said fibrils or aggregates; and
    - (b) detecting whether said fibrils or aggregates are retained on said filter
  2. The method of claim 1 wherein said amyloid-like fibrils or protein aggregates are indicative of a disease.
  3. The method of claim 2 wherein said disease is a human disease.
  4. The method of claim 2 or 3 wherein said disease is associated with a polyglutamine expansion.
  5. The method of any one of claims 2 to 4 wherein said disease is Huntington's disease, spinal and bulbar muscular atrophy, dentatorubral pallidoluysian atrophy, spinocerebellar ataxia type-1, -2, -3, -6 or -7, Alzheimer disease, BSE, primary systemic amyloidosis, secondary systemic amyloidosis, senile systemic amyloidosis, familial amyloid polyneuropathy I, hereditary cerebral amyloid angiopathy, hemodialysis-related amyloidosis, familial amyloid polyneuropathy III, Finnish hereditary systemic amyloidosis, type II diabetes, medullary carcinoma of the thyroid, spongiform encephalopathies: Kuru, Gerstmann-Sträussler-Scheinker syndrome (GSS), familial insomnia, scrapie, atrial amyloidosis, hereditary non-neuropathic systemic amyloidosis, injection-localized amyloidosis, hereditary renal amyloidosis, or Parkinson's disease.
  6. The method of any one of claims 1 to 5 wherein said filter is comprised of material with low protein adsorption.
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7. The method of claim 6 wherein said material with low protein adsorption is cellulose acetate.
8. The method of any one of claims 1 to 7 wherein, prior to step (b), the following step is carried out:  
(b') washing said filter so as to remove detergent- or urea-soluble material.
9. The method of any one of claims 1 to 8 wherein detergent- or urea-soluble material is simultaneously with or subsequent to step (a), sucked through said filter.
10. The method of any one of claims 1 to 9 wherein detection in step (b) is effected by an antibody, or (poly)peptide, preferably a tag or an enzyme, or a fragment or derivative thereof or a chemical reagent that specifically binds to said fibrils or aggregates.
11. The method of any one of claims 1 to 9 wherein detection in step (b) is effected by electron microscopy, electron scanning microscopy, fluorescence or chemiluminescence.
12. The method of any one of claims 1 to 11 wherein said material is derived from tissues or cells of bacteria, yeast, fungi, plants, insects, animals, preferably mammals, humans, from a transgenic animal or a transgenic plant.
13. The method of any one of claims 1 to 11 further comprising the following steps prior to step (a):  
(a') incubating a fusion protein comprising a (poly)peptide that enhances solubility and/or prevents aggregation of said fusion protein, an amyloidogenic (poly)peptide that has the ability to self-assemble into amyloid-like fibrils or protein aggregates when released from said fusion protein and a cleavable site that separates the above-mentioned components of the fusion protein in the presence of a suspected inhibitor of amyloid-like fibril or protein aggregate formation; and

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~~(a'')~~ simultaneously with or after step (a'), further incubating with a compound that induces cleavage at said cleavage site.

14. The method of claim 13 wherein said cleavable site is an enzymatically cleavable site or a chemically cleavable site or a site cleavable by intein self-cleavage in the presence of thiols.

sub B4  
15. The method of claim 13 or 14 further comprising, prior to step (b) and after step (a''):

(a''') incubation with an inhibitor of said compound that induces cleavage.

16. The method of any one of claims 13 to 15 wherein said amyloidogenic (poly)peptide comprises a polyglutamine expansion.

17. The method of any one of claims 4 to 16 wherein said polyglutamine expansion comprises at least 35, preferably at least 41, more preferably at least 48 and most preferably at least 51 glutamines.

18. The method of any one of claims 1 to 17 wherein said contacting is effected by dotting, spotting or pipetting said material onto said filter.

19. The method of any one of claims 1 to 18 wherein said filter is a filter membrane.

20. The method of any one of claims 1 to 19 wherein said detergent is SDS or Triton X-100.

21. An inhibitor identified by the method of any one of claims 13 to 19.

22. — The inhibitor of claim 21 which is an antibody or a derivative or functional fragment thereof, a peptide or a chemical reagent.

23. A pharmaceutical composition comprising the inhibitor of claim 21 to 22 and a pharmaceutically acceptable carrier and/or diluent.

24. A diagnostic composition comprising  
(i) a fusion protein as defined in any one of the preceding claims.

25.

The diagnostic composition of claim 24 further comprising

- (ii) a filter as defined in any one of the preceding claims optionally or preferably contained in a microtiter plate; and optionally
- (iii) a compound that induces cleavage as defined in any one of the preceding claims; and optionally
- (iv) an inhibitor of said compound of (c); and optionally
- (v) suitable buffer solutions.

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